AMENDMENTS TO THE SPECIFICATION

Please amend the Title as follows:

~~Crystallization of ISPA~~ A Crystalline Composition of Farsenyl Pyrophosphate Synthase (IspA)

Please amend the Abstract as follows:

[00187] Provided are crystals relating to Farsenyl Pyrophosphate Synthase (IspA) from E. coli and its various uses.

Please delete paragraph [00180].

Please amend paragraphs [0035], [0046], [0070], [0080], [00178] and [00183] as follows:

[0035] Figure 3 lists a set of atomic structure coordinates for IspA (the amino acid numbers of column E correlate to residues 16-314 of SEQ. ID No. 1) as derived by X-ray crystallography from a crystal that comprises the protein. The following abbreviations are used in Figure 3: "X, Y, Z" crystallographically define the atomic position of the element measured; "B" is a thermal factor that measures movement of the atom around its atomic center; "Occ" is an occupancy factor that refers to the fraction of the molecules in which each atom occupies the position specified by the coordinates (a value of "1" indicates that each atom has the same conformation, i.e., the same position, in all molecules of the crystal).

[0046] In one embodiment, IspA comprises the E. coli form of full length IspA ~~set forth herein as~~ (residues 16-314 of SEQ. ID No. 1) (GenBank Accession Number NM_ D00694) with an N-terminal His-tag (MGSDKIIHHHHHHHTL (residues 1-15 of SEQ ID No: 1).

[0070] The gene encoding IspA can be isolated from RNA, cDNA or cDNA libraries. In this case, the portion of the gene encoding amino acid residues 16-314 (SEQ. ID No. 1), corresponding to E. coli IspA, was isolated and is shown as residues 46-945 of SEQ. ID No. 2.

[0080] It should be understood that forming crystals comprising IspA and crystals comprising IspA according to the invention are not intended to be limited to the E. coli form of IspA shown in SEQ. ID No. 1~~, fragments comprising residues 16-314 of SEQ. ID No. 1~~ and fragments comprising residues 16-314 of SEQ. ID No. 1. Rather, it should be recognized that the invention may be extended to various other fragments and variants of wild-type IspA as described above.

[00178] The gene encoding residues ~~1-299 (from~~ 16-314 of SEQ. ID No. 1~~)~~, which corresponds to the full-length IspA from E.coli, was isolated by PCR from E. coli genomic DNA (DH10B-1r strain) and cloned into the TOPO-activated cloning site of pSX28 vector. This DNA sequence along with residues encoding the N-terminal His-tag (residues 1-15 of SEQ ID No: 1) is presented in SEQ. ID No. 2. Expression of SEQ. ID No:2 in ~~this~~ the pSX28 vector generated a fusion of the full-length IspA with a non-cleavable amino-terminal six histidine tag (SEQ ID No: 1). ~~, the~~ The amino acid sequence of the tag ~~which~~ is shown, underlined, in Figure 1 (residues 1-15 of SEQ. ID No.~~3~~ 1).

[00183] IspA protein samples (corresponding to residues 1-314 of SEQ. ID No. 1) were concentrated to the final concentration of 12mg/ml, incubated with 0.5-2.50 mM $MgCl_2$ and ligands before initiating crystallization trials. Several combinations of ligands in the 0.5-2.5mM range produced crystals useful for structural analysis. The ligand combinations included: 1) isopentyl pyrophosphate (IPP) + dimethylallyl S-thiolodiphosphate (DMASPP), 2) IPP + farnesyl S-thiolodiphosphate (FSPP), 3) geranyl diphosphate (GPP), 4) IPP + geranyl S-thiolodiphosphate, 5) IPP + Risedronate, 6) IPP + Pamidronate, and 7) Risedronate. Interestingly, it was found that crystallization was facilitated by the presence of ligands.